



**UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/837,840	04/22/97	ZIRRIA	B

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HM32/0511

EXAMINER

KUNZ, G

ART UNIT

1623

PAPER NUMBER

DATE MAILED: 05/11/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

Applicant(s)

Examiner

Group Art Unit

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 4-22-97.
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 1-20 is/are pending in the application.
- Of the above claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 1-20 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____.
 - ☐ received in this national stage application from the International Bureau (PCT Rule 1.7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☒ Notice of References Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other _____

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 - 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zikria (4,994,444) in view of Weiss (J. Biol. Chem. 255 (20): 9912-9917, 1980), Munkes et al. (EMBase Abstr. 841469), and Gerdin et al. (Chem. Abstr. 1983:447701)

Claims 1 - 19 are directed to a method for treating a human to prevent leakage of serum proteins from capillary endothelial junctions comprising administering a composition containing hydroxyethyl starch or hydroxyethyl dextran and at least one antioxidant selected from the group consisting of superoxide dismutase, glutathione peroxidase, catalase, hydroxyethyl rutoside, cyclic adenosine monophosphate, and vitamin C. Claim 20 is directed to the composition used in the aforementioned method.

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Zikria teaches the use of hydroxyethyl starch and hydroxyethyl dextran as a means for treating a human subject to prevent leakage of serum proteins from capillary endothelial junctions (See abstract, columns 1 - 2, and claims 1 - 12). Zikria does not teach the use of antioxidants along with the hydroxyethyl starch or hydroxyethyl dextran.

However, Weiss teaches that exogenous superoxide dismutase can protect human red blood cells from the oxidative damage of superoxide anion produced by neutrophils. This reference further teaches that catalase and glutathione peroxidase are enzymes which can reduce the oxidizing species, hydrogen peroxide to less harmful molecules. Thus, the artisan would take from this reference the clear message that oxidation can damage cells and that molecules which disarm oxidants, i.e., antioxidants, should help protect the integrity of cells.

While neither Zikria nor Weiss mentions the role of cAMP in protecting cells from oxidative damage, Munkres et al. does teach that dietary cAMP helps to induce superoxide dismutase in short-lived mutants of Neurospora. In this case, cAMP induces the production of superoxide dismutase. The authors hypothesize that dietary antioxidants may enhance the survival of Neurospora by supplanting the function of any deficient antioxygenic enzymes.

While neither Zikria nor Weiss nor Munkres teaches the value of hydroxyethyl rutoside, Gerdin does teach that hydroxyethyl rutoside acts as an antioxidant to prevent leakage of serum proteins from capillary endothelial junctions.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time of the invention to have modified the teachings of Zikria by adding any art-recognized non-toxic

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antioxidant molecule, such as vitamin C, superoxide dismutase, catalase, glutathione peroxidase, hydroxethyl rutoside, or cAMP (as suggested by Weiss, Munkres, and Gerdin) for the expressed purpose of protecting capillary endothelial junctions from oxidative damage that would lead to leakage of serum proteins. The use of Ringer's lactate solution as a base for this composition is obvious because this is a standard IV isotonic solution that is described by Zikria in column 2, lines 9 - 13). The necessary concentration of the hydroxyethyl dextran or starch is also taught by Zikria as about 6% (column 10, lines 3-6). The concentrations of each of the antioxidants are either well known in the art or can be readily determined in amounts below the toxic threshold. Consequently, the instantly claimed method for preventing leakage of serum proteins from capillary endothelial junctions and the corresponding compositions is prima facie obvious in the absence of clear and convincing evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kunz, whose telephone number is (703) 308-4623. The examiner can normally be reached on Tuesday through Friday from 6:30 AM to 4:00 PM. The examiner can also be reached on alternate Mondays.

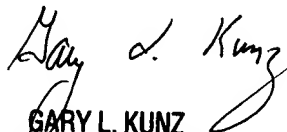
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marion Knode, can be reached on (703) 308-4311. The fax phone number for this Group is (703) 308-4556.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.


GARY L. KUNZ
PRIMARY EXAMINER
GROUP 1200